* * * * STN Columbus

FILE 'HOME' ENTERED AT 11:08:55 ON 19 JAN 2007

=> file caplus CA COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 11:09:39 ON 19 JAN 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'CA' ENTERED AT 11:09:39 ON 19 JAN 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> Retinoid acid

406 RETINOID ACID

=> selenium or selenium salt

176498 SELENIUM OR SELENIUM SALT

=> L1 and L2

4 L1 AND L2

=> D L3 IBIB ABS 1-4

ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1331259 CAPLUS

DOCUMENT NUMBER:

144:64327

Use of selenium or a selenium TITLE:

salt and a retinoid acid

or a retinoid in the treatment of viral hepatitis C

INVENTOR (S): Herget, Thomas; Klebl, Bert PATENT ASSIGNEE(S): GPC Biotech A.-G., Germany SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATI	ENT :	NO.			KIND		DATE			APPL	ICAT		DATE				
				•	-	-					-				-	- -	
WO 2	2005	1204	79		A1		2005	1222	1	WO 2	005-1	EP62	26		2	0050	609
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		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KP,	KR,	KZ,
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,
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PRIORITY APPLN. INFO.: US 2004-578161P

The present invention relates to combination therapies comprising at least one retinoid or retinoid agonist together with selenium or a selenium salt particularly useful in conjunction with

conventional antiviral therapeutics which are synergistically effective against Hepatitis C virus (HCV) infections. In particular, the present invention relates to the synergism between compds. capable of activating or upregulating the gastrointestinal form of glutathione peroxidase for prophylaxis and/or treatment of HCV infections, administered in combination therapies with interferons. The combinations disclosed have proven surprisingly effective even in patients unresponsive to interferon/ribavirin therapies.

REFERENCE COUNT: THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS 8 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER: 2005:1210008 CAPLUS

DOCUMENT NUMBER: 144:16623

TITLE: The effect of all-trans retinoic acid and sodium

selenite (Na2SeO3) on VEGF and its receptor expression

in HL-60 cells

AUTHOR(S): Ye, Jin; Liu, Fu-qiang; Wu, Yi-ping

CORPORATE SOURCE: Department of Hematology, Beijing Tongren Hospital,

Capital University of Medical Science, Beijing,

100730, Peop. Rep. China

SOURCE: Zhongguo Shiyan Xueyexue Zazhi (2004), 12(2), 142-146

CODEN: ZSXZAF; ISSN: 1009-2137

PUBLISHER: Zhongguo Shiyan Xueyexue Zazhishe

DOCUMENT TYPE: Journal LANGUAGE: Chinese

In order to investigate the effect of non-medullar toxicity drug - all AB trans retinoid acid (ATRA) and cancer preventive trace element-selenium compound - sodium selenite (Na2Se3) on the expression of vascular endothelial growth factor (VEGF) and its receptor in HL-60 cells, the expression of VEGF and its receptor in HL-60 cells were detected by ELISA technique and flow cytometry before and after treatment with two drugs. The results showed that the mean VEGF concns. in the cultural supernatant of 5 and 10 µmol/L ATRA-treated HL-60 cells for 48 and 72 h were lower than those of the control group without adding ATRA. The differences between the ATRA-treated groups and the control group were statistically significant (P = 0.001, P = 0.000, P < 0.01, resp.). The levels of VEGF-R on the surface of HL-60 cells also decreased after treatment with ATRA of 5 and 10 μ mol/L for 72 h, but at 48 h the expression rates of VEGF-R on HL-60 cells of the two ATRA treated groups were not significantly decreased. At 48 and 72 h, Na1SeO3 of 5 and 10 µmol/L had no obvious effect on HL-60 secreting VEGF, but notablely inhibited the expression of VEGF-R. In conclusion, ATRA could inhibit the expression of VEGF and its receptor in HL-60 cell. Na2SeO3 could not inhibit the expression of VEGF in HL-60 cell, but could decrease the receptor expression of VEGF, which mechanism should be further studied. ATRA and Na2SeO3 had not obvious medullar- inhibition, but anti-angiogenesis activity. It is suggested that combination of two drugs with conventional therapy may enhance the effect of radiotherapy and chemotherapy, and reduce the dose and thus toxicity of chemotherapeutic agents.

ANSWER 3 OF 4 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 144:64327 CA

TITLE: Use of selenium or a selenium

salt and a retinoid acid

or a retinoid in the treatment of viral hepatitis C

INVENTOR(S): Herget, Thomas; Klebl, Bert PATENT ASSIGNEE(S): GPC Biotech A.-G., Germany SOURCE:

PCT Int. Appl., 58 pp.

CODEN: PIXXD2 DOCUMENT TYPE:

Patent LANGUAGE: English FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
                 KIND DATE
                                  APPLICATION NO.
                                                         DATE
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                  A1 20051222 WO 2005-EP6226
WO 2005120479
                                                         20050609
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       CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
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       RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
       MR, NE, SN, TD, TG
                                   US 2004-578161P
                                                     P 20040609
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PRIORITY APPLN. INFO.:

The present invention relates to combination therapies comprising at least one retinoid or retinoid agonist together with selenium or a selenium salt particularly useful in conjunction with conventional antiviral therapeutics which are synergistically effective against Hepatitis C virus (HCV) infections. In particular, the present invention relates to the synergism between compds. capable of activating or upregulating the gastrointestinal form of glutathione peroxidase for prophylaxis and/or treatment of HCV infections, administered in combination therapies with interferons. The combinations disclosed have proven surprisingly effective even in patients unresponsive to interferon/ribavirin therapies.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 4 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

144:16623 CA

TITLE:

The effect of all-trans retinoic acid and sodium

selenite (Na2SeO3) on VEGF and its receptor expression

in HL-60 cells

AUTHOR(S):

Ye, Jin; Liu, Fu-qiang; Wu, Yi-ping

CORPORATE SOURCE:

Department of Hematology, Beijing Tongren Hospital,

Capital University of Medical Science, Beijing,

100730, Peop. Rep. China

SOURCE:

Zhongguo Shiyan Xueyexue Zazhi (2004), 12(2), 142-146

CODEN: ZSXZAF; ISSN: 1009-2137

PUBLISHER:

Zhongguo Shiyan Xueyexue Zazhishe

Journal

DOCUMENT TYPE: LANGUAGE: Chinese

In order to investigate the effect of non-medullar toxicity drug - all trans retinoid acid (ATRA) and cancer preventive trace element-selenium compound - sodium selenite (Na2Se3) on the expression of vascular endothelial growth factor (VEGF) and its receptor in HL-60 cells, the expression of VEGF and its receptor in HL-60 cells were detected by ELISA technique and flow cytometry before and after treatment with two drugs. The results showed that the mean VEGF concns. in the cultural supernatant of 5 and 10 μ mol/L ATRA-treated HL-60 cells for 48 and 72 h were lower than those of the control group without adding ATRA. The differences between the ATRA-treated groups and the control group were statistically significant (P = 0.001, P = 0.000, P < 0.01, resp.). The levels of VEGF-R on the surface of HL-60 cells also decreased after treatment with ATRA of 5 and 10 µmol/L for 72 h, but at 48 h the expression rates of VEGF-R on HL-60 cells of the two ATRA treated groups were not significantly decreased. At 48 and 72 h, Na1SeO3 of 5 and 10 µmol/L had no obvious effect on HL-60 secreting VEGF, but notablely inhibited the expression of VEGF-R. In conclusion, ATRA could inhibit the expression of VEGF and its receptor in HL-60 cell. Na2SeO3 could not

inhibit the expression of VEGF in HL-60 cell, but could decrease the receptor expression of VEGF, which mechanism should be further studied. ATRA and Na2SeO3 had not obvious medullar- inhibition, but anti-angiogenesis activity. It is suggested that combination of two drugs with conventional therapy may enhance the effect of radiotherapy and chemotherapy, and reduce the dose and thus toxicity of chemotherapeutic agents.

=> D L4 IBIB ABS 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1331259 CAPLUS

DOCUMENT NUMBER: 144:64327

TITLE: Use of selenium or a selenium salt and a

retinoid acid or a retinoid in the treatment of viral hepatitis C

INVENTOR(S): Herget, Thomas; Klebl, Bert PATENT ASSIGNEE(S): GPC Biotech A.-G., Germany SOURCE: PCT Int. Appl., 58 pp.

OURCE: PCT Int. Appl., 58 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
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               KIND
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WO 2005120479 Δ1
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                        20051222 WO 2005-EP6226
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       MR, NE, SN, TD, TG
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PRIORITY APPLN. INFO.:

US 2004-578161P P 20040609

The present invention relates to combination therapies comprising at least one retinoid or retinoid agonist together with selenium or a selenium salt particularly useful in conjunction with conventional antiviral therapeutics which are synergistically effective against Hepatitis C virus (HCV) infections. In particular, the present invention relates to the synergism between compds. capable of activating or upregulating the gastrointestinal form of glutathione peroxidase for prophylaxis and/or treatment of HCV infections, administered in combination therapies with interferons. The combinations disclosed have proven surprisingly effective even in patients unresponsive to interferon/ribavirin therapies.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CA COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 144:64327 CA

```
TITLE:
                        Use of selenium or a selenium salt and a
                         retinoid acid or a retinoid in the
                         treatment of viral hepatitis C
INVENTOR(S):
                        Herget, Thomas; Klebl, Bert
                        GPC Biotech A.-G., Germany
PATENT ASSIGNEE(S):
SOURCE:
                         PCT Int. Appl., 58 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                       KIND
                               DATE
                                          APPLICATION NO.
     WO 2005120479 A1 000
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                        A1 20051222 WO 2005-EP6226
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             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
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             MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                           US 2004-578161P
                                                             P 20040609
     The present invention relates to combination therapies comprising at least
     one retinoid or retinoid agonist together with selenium or a selenium salt
     particularly useful in conjunction with conventional antiviral
     therapeutics which are synergistically effective against Hepatitis C virus
     (HCV) infections. In particular, the present invention relates
     to the synergism between compds. capable of activating or upregulating the
     gastrointestinal form of glutathione peroxidase for prophylaxis and/or
     treatment of HCV infections, administered in combination
     therapies with interferons. The combinations disclosed have proven
     surprisingly effective even in patients unresponsive to
     interferon/ribavirin therapies.
REFERENCE COUNT:
                        8
                              THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
                              RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> "6-[3-(1-adamantyl)-4-hydroxyphenyl]-2-naphthalene carboxylic acid"
            86 "6-[3-(1-ADAMANTYL)-4-HYDROXYPHENYL]-2-NAPHTHALENE CARBOXYLIC
=> retinoid and L6
           86 RETINOID AND L6
=> HCV and L7
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L8
=> D L8 IBIB ABS 1-2
    ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
                        2004:490732 CAPLUS
DOCUMENT NUMBER:
                        141:42933
TITLE:
                        Formulations useful against hepatitis C virus
                        infections
INVENTOR(S):
                        Herget, Thomas; Klebl, Bert
PATENT ASSIGNEE(S):
                       Axxima Pharmaceuticals A.-G., Germany
SOURCE:
                        PCT Int. Appl., 72 pp.
                        CODEN: PIXXD2
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DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

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PATENT NO.
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    WO 2004050101
                        A2
                               20040617
                                          WO 2003-EP13514
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                                          US 2003-446246P
                                          WO 2003-EP13514
                                                             W 20031201
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The present invention relates generally to chemical compds. and substances AB which are effective against Hepatitis C virus (HCV) infections. Moreover, the present invention relates to compns. comprising said compds. and/or substances, to methods for preventing HCV infections as well use of the compds. and/or substances for the preparation of compns. useful for the prophylaxis and/or treatment of HCV infections. Useful compds. and substances according to the invention are selenium, selenium salts, Vitamin D3 and retinoids, like all trans retinoic acid and salts thereof, C1-C10 alkyl amide of all trans retinoic acid and salts thereof, C1-C10 alkyl esters of all trans retinoic acid and salts thereof, 9-cis retinoic acid and salts thereof, C1-C10 alkyl amide of 9-cis retinoic acid and salts thereof, C1-C10 alkyl esters of 9-cis retinoic acid and salts thereof, (E)-4-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetra methyl-2-naphthalenyl-1)-propenyl] benzoic acid (TTNPB), (4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl] carboxamido) benzoic acid (AM-580), N-(4-hydroxyphenyl) retinamide (4-HPR), and 6-[3-(1-adamantyl)-4hydroxyphenyl]-2-naphthalene carboxylic acid (AHPN).

ANSWER 2 OF 2 CA COPYRIGHT 2007 ACS on STN

LO ANSWER 2 OF 2 CA COPIE

ACCESSION NUMBER: 141:42933 CA

TITLE: Formulations useful against hepatitis C virus

infections

INVENTOR(S):
Herget, Thomas; Klebl, Bert

PATENT ASSIGNEE(S): Axxima Pharmaceuticals A.-G., Germany

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

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                                                             P 20021203
                                           US 2002-430367P
                                           DE 2003-10305138
                                                             A 20030207
                                                              P 20030211
                                           US 2003-446246P
                                           WO 2003-EP13514
                                                              W 20031201
     The present invention relates generally to chemical compds. and substances
AB
    which are effective against Hepatitis C virus (HCV) infections.
    Moreover, the present invention relates to compns. comprising said compds.
    and/or substances, to methods for preventing HCV infections as.
    well use of the compds. and/or substances for the preparation of compns. useful
     for the prophylaxis and/or treatment of HCV infections. Useful
     compds. and substances according to the invention are selenium, selenium
     salts, Vitamin D3 and retinoids, like all trans retinoic acid
    and salts thereof, C1-C10 alkyl amide of all trans retinoic acid and salts
    thereof, C1-C10 alkyl esters of all trans retinoic acid and salts thereof,
     9-cis retinoic acid and salts thereof, C1-C10 alkyl amide of 9-cis
    retinoic acid and salts thereof, C1-C10 alkyl esters of 9-cis retinoic
    acid and salts thereof, (E)-4-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetra
    methyl-2-naphthalenyl-1)-propenyl] benzoic acid (TTNPB),
     (4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl] carboxamido)
    benzoic acid (AM-580), N-(4-hydroxyphenyl) retinamide (4-HPR), and
    6-[3-(1-adamantyl)-4-
    hydroxyphenyl]-2-naphthalene
    carboxylic acid (AHPN).
=> "gastrointestinal glutathione peroxidase"
           65 "GASTROINTESTINAL GLUTATHIONE PEROXIDASE"
=> L9 and L8
L10
            0 L9 AND L8
=> L9 and selenium
```

=> L12 and L8

=> "glutathion peroxidase"

48 L9 AND SELENIUM

154 "GLUTATHION PEROXIDASE"

L11

```
L13
```

0 L12 AND L8

=> selenium adj salt

0 SELENIUM ADJ SALT L14

=> selenium (w) salt

L15 413 SELENIUM (W) SALT

=> L15 and L8

2 L15 AND L8 L16

=> L15 and L9

L17 2 L15 AND L9

=> L15 and HCV

L18 6 L15 AND HCV

=> D L18 IBIBI ABS 1-6

'IBIBI' IS NOT A VALID FORMAT

In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.

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L18 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:1331259 CAPLUS

DOCUMENT NUMBER:

144:64327

TITLE:

Use of selenium or a selenium salt

and a retinoid acid or a retinoid in the treatment of

viral hepatitis C

INVENTOR(S):

Herget, Thomas; Klebl, Bert GPC Biotech A.-G., Germany

PATENT ASSIGNEE(S):

PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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WO	2005	1204	70		7.1	-	2005	1222	,						2	0050	

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L18 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:633154 CAPLUS

DOCUMENT NUMBER:

141:167729

TITLE:

Gastrointestinal glutathione peroxidase as therapeutic

target for treatment of HCV infection,

methods of treating HCV infection, and

compounds useful therefor

INVENTOR(S): Herget, Thomas; Cotten, Matthew; Obert, Sabine; Klebl,

Bert

PATENT ASSIGNEE(S): Germany

SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.

Pat. Appl. 2003 180,719.

CODEN: USXXCO

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

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L18 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2004:490732 CAPLUS

DOCUMENT NUMBER:

141:42933

TITLE:

Formulations useful against hepatitis C virus

infections

INVENTOR(S):

Herget, Thomas; Klebl, Bert

PATENT ASSIGNEE(S):

Axxima Pharmaceuticals A.-G., Germany

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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L18 ANSWER 4 OF 6 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 14

144:64327 CA

TITLE:

Use of selenium or a selenium salt

and a retinoid acid or a retinoid in the treatment of

viral hepatitis C

INVENTOR(S): Herget, Thomas; Klebl, Bert PATENT ASSIGNEE(S): GPC Biotech A.-G., Germany SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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US 2004-578161P P 20040609

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8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 6 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

141:167729 CA

TITLE:

Gastrointestinal glutathione peroxidase as therapeutic

target for treatment of HCV infection, methods of treating HCV infection, and

compounds useful therefor

INVENTOR(S):

Herget, Thomas; Cotten, Matthew; Obert, Sabine; Klebl,

Bert

PATENT ASSIGNEE(S):

Germany

SOURCE:

U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.

Pat. Appl. 2003 180,719.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

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L18 ANSWER 6 OF 6 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

141:42933 CA

CODEN: PIXXD2

TITLE:

Formulations useful against hepatitis C virus

infections

INVENTOR(S):

Herget, Thomas; Klebl, Bert

PATENT ASSIGNEE(S):

Axxima Pharmaceuticals A.-G., Germany

PCT Int. Appl., 72 pp.

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

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WO 2004050101 WO 2004050101	A2 20040617	WO 2003-EP13514	20031201
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PRIORITY APPLN. INFO	· :	DE 2002-10255861 US 2002-430367P DE 2003-10305138 US 2003-446246P	P 20021203 A 20030207

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L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:490732 CAPLUS

DOCUMENT NUMBER: 141:42933

TITLE: Formulations useful against hepatitis C virus

infections

INVENTOR(S): Herget, Thomas; Klebl, Bert

PATENT ASSIGNEE(S): Axxima Pharmaceuticals A.-G., Germany

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

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LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

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AB The present invention relates generally to chemical compds. and substances which are effective against Hepatitis C virus (HCV) infections. Moreover, the present invention relates to compns. comprising said compds. and/or substances, to methods for preventing HCV infections as well use of the compds. and/or substances for the preparation of compns. useful for the prophylaxis and/or treatment of HCV infections. Useful compds. and substances according to the invention are selenium, selenium salts, Vitamin D3 and retinoids, like all trans retinoic acid and salts thereof, C1-C10 alkyl amide of all trans retinoic acid and salts thereof, C1-C10 alkyl esters of all trans retinoic acid and salts thereof, 9-cis retinoic acid and salts thereof, C1-C10 alkyl amide of 9-cis retinoic acid and salts thereof, C1-C10 alkyl esters of 9-cis retinoic acid and salts thereof, (E)-4-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetra methyl-2-naphthalenyl-1)-propenyl] benzoic acid (TTNPB), (4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl] carboxamido) benzoic acid (AM-580), N-(4-hydroxyphenyl) retinamide (4-HPR), and 6-[3-(1-adamantyl)-4hydroxyphenyl]-2-naphthalene carboxylic acid (AHPN).

L16 ANSWER 2 OF 2 CA COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 141:42933 CA

TITLE: Formulations useful against hepatitis C virus

infections

INVENTOR(S):
Herget, Thomas; Klebl, Bert

PATENT ASSIGNEE(S): Axxima Pharmaceuticals A.-G., Germany

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

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The present invention relates generally to chemical compds. and substances AB which are effective against Hepatitis C virus (HCV) infections. Moreover, the present invention relates to compns. comprising said compds. and/or substances, to methods for preventing HCV infections as well use of the compds. and/or substances for the preparation of compns. useful for the prophylaxis and/or treatment of HCV infections. Useful compds. and substances according to the invention are selenium, selenium salts, Vitamin D3 and retinoids, like all trans retinoic acid and salts thereof, C1-C10 alkyl amide of all trans retinoic acid and salts thereof, C1-C10 alkyl esters of all trans retinoic acid and salts thereof, 9-cis retinoic acid and salts thereof, C1-C10 alkyl amide of 9-cis retinoic acid and salts thereof, C1-C10 alkyl esters of 9-cis retinoic acid and salts thereof, (E)-4-[2-(5,6,7,8-tetrahydro-5,5,8,8-tetra methyl-2-naphthalenyl-1)-propenyl] benzoic acid (TTNPB), (4-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl] carboxamido) benzoic acid (AM-580), N-(4-hydroxyphenyl) retinamide (4-HPR), and 6-[3-(1-adamantyl)-4hydroxyphenyl]-2-naphthalene carboxylic acid (AHPN).

L17 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:633154 CAPLUS

DOCUMENT NUMBER: 141:167729

TITLE: Gastrointestinal glutathione

peroxidase as therapeutic target for treatment

of HCV infection, methods of treating HCV infection,

and compounds useful therefor

INVENTOR(S): Herget, Thomas; Cotten, Matthew; Obert, Sabine; Klebl,

Bert

PATENT ASSIGNEE(S): Germany

SOURCE: U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.

Pat. Appl. 2003 180,719.

CODEN: USXXCO

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

P	PAT	ENT 1	NO.			KIND DATE					APPL	ICAT:	DATE					
Ü	JS	2004	1520	73				2004	0805	1	US 2	003-	7237	19		20	0031	126
W	10	2002	0842	94		A2		2002	1024	1	WO 2	002-	EP41	67		20	00204	415
W	10	2002	0842	94		A3		2003	1030									
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	ВG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
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			GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG		•	-	•	•	•	•
D	Œ	1025	5861			A1		2004	0617	1	DE 2	002-		20	0021	129		
U	JS	2003	1807	19		A1		2003	0925	1	US 2	003-3		20	0030	114		
PRIORI	TY	APP	LN.	INFO	. :					US 2001-283345P						P 20	00104	413
										1	WO 2	002-1	EP41	67	7	A2 20	00204	415
										1	DE 2	002-	1025	5861	7	A 20	0021	129
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The present invention relates to the human cellular protein glutathione AR peroxidase-gastrointestinal as a target for medical intervention against Hepatitis C virus (HCV) infections. Furthermore, the present invention relates to a method for the detection of compds. useful for prophylaxis and/or treatment of hepatitis C virus infections and a method for detecting hepatitis C virus infections in an individual or in cells. compns., compds., nucleic acid mols. (such as aptamers), mono- or polyclonal antibodies are disclosed which are effective for the treatment of HCV infections, and methods for prophylaxis and/or treatment of hepatitis C virus infections or for the regulation of hepatitis C virus production are disclosed. The inventors designed a randomized, single-blinded clin. study to test the safety, tolerability, and efficacy of all-trans retinoic acid alone or in combination with pegylated α interferon in patients with chronic hepatitis C. The therapy regimens include: Vesanoid (orally administered all-trans retinoic acid compound, Hoffman-La Roche); Pegasys (slow-release pegylated interferon α2a, Hoffman-La Roche); and selen 30 ALLACT (supplement containing selenium and ALLACT composed of garlic powder and Lactobacillus bulgaricus).

TITLE:

Gastrointestinal glutathione

peroxidase as therapeutic target for treatment

of HCV infection, methods of treating HCV infection,

and compounds useful therefor

INVENTOR(S):

Herget, Thomas; Cotten, Matthew; Obert, Sabine; Klebl,

Bert

PATENT ASSIGNEE(S):

Germany

SOURCE:

U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S.

Pat. Appl. 2003 180,719.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	TENT 1	NO.			KIND DATE						ICAT:		DATE				
HC	2004	1520	72				2004	0005							2	2021	106
	2004															0031	
WO	2002	0842	94		A2		2002	1024	1	WO 2	002-1	EP41	67		2	00204	415
WO	2002	0842	94		A3		2003:	1030									
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	ΒA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
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DE	1025	5861			A1		2004	0617	.]	DE 2	002-	1025	5861		26	0021	129
US	2003	1807	19		A1		2003	0925	1	JS 2	003-		20	0030	114		
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AB The present invention relates to the human cellular protein glutathione peroxidase-gastrointestinal as a target for medical intervention against Hepatitis C virus (HCV) infections. Furthermore, the present invention relates to a method for the detection of compds. useful for prophylaxis and/or treatment of hepatitis C virus infections and a method for detecting hepatitis C virus infections in an individual or in cells. compns., compds., nucleic acid mols. (such as aptamers), mono- or polyclonal antibodies are disclosed which are effective for the treatment of HCV infections, and methods for prophylaxis and/or treatment of hepatitis C virus infections or for the regulation of hepatitis C virus production are disclosed. The inventors designed a randomized, single-blinded clin. study to test the safety, tolerability, and efficacy of all-trans retinoic acid alone or in combination with pegylated α interferon in patients with chronic hepatitis C. The therapy regimens include: Vesanoid (orally administered all-trans retinoic acid compound, Hoffman-La Roche); Pegasys (slow-release pegylated interferon α2a, Hoffman-La Roche); and selen 30 ALLACT (supplement containing selenium and ALLACT composed of garlic powder and Lactobacillus bulgaricus).

L18 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:344067 BIOSIS DOCUMENT NUMBER: PREV200600343199

TITLE: Hepatitis C (HCV) and antioxidant deficiency in

HIV plus drug users in Miami.

AUTHOR(S): Baum, Marianna K. [Reprint Author]; Duan, Rui; Sales,

Sabrina; Rafie, Carlin; Carroll, Linda Ann; Campa, Adriana

CORPORATE SOURCE: Florida Int Univ, Miami, FL 33199 USA

SOURCE: FASEB Journal, (MAR 6 2006) Vol. 20, No. 4, Part 1, pp.

A145.

Meeting Info.: Experimental Biology 2006 Meeting. San Francisco, CA, USA. April 01 -05, 2006. Amer Assoc

Anatomists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol;

Amer Soc Investigat Pathol; Amer Soc Nutr; Amer Soc

Pharmacol & Expt Therapeut. CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Jul 2006

Last Updated on STN: 12 Jul 2006

Objective: Increased oxidative stress is common in HIV and HCV infections, complicated by secondary malnutrition which may heighten oxidative stress. We examined antioxidant status in HIV/HCV coinfection in HIV+ drug users. Method: After consenting 207 HIV+ drug users, demographic, nutritional, medical and treatment questionnaires and anthropometries were completed. Blood was drawn for CD4 cell counts, HIV viral load, serum chemistry and plasma zinc and selenium. Results: Of the 207 participants, 37.2% were HCV coinfected, 72.5 % were males; mean age was 42. In the co-infected group, as compared to HIV+, mean plasma zinc (0.61 +/- 0.13 vs. 0.67 +/- 0.15 mg/L), and median serum albumin [4.0 (0.4-5.1) vs. 3.9 (2.7-4.8) g/dL, p=0.04)] were significantly lower, while mean values of liver enzymes (AST: 55.3 +/- 42 vs. 35 30 IU/L, p < 0.001; ALT: 50.2 +/- 50 vs. 33 44 IU/L, p=0.003; LDH: 209 53 vs. 197 44 IU/L, p=0.02) were higher, after adjusting for age, gender, CD4 count, viral load and HAART. Lower % of participants with plasma selenium > 100 mg/dL, (85.7 vs. 94.4, p=0.056), and lower intake of vitamin E (1.5 + / - 2.4 vs. 2.3 + / - 2.8 mg)p=0.05) and thiamin (1.5 +/- 1.3 vs. 1.8 +/- 1.2 mg, p=0.04) was observed in the coinfected group. No significant differences were found in BMI, calories, macronutrients and beta-carotene between the 2 groups.Conclusion: HIV/HCV co-infected persons are in a poorer antioxidant status than those who are HIV+, as suggested by lower plasma zinc and selenium, and lower intake of vitamin E and thiamin. Coinfection is strongly associated with liver dysfunction as shown by lower albumin and higher ALT, AST and LDH. Studies on association of antioxidants and HIV/HCV co-infection are neede

L22 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:210744 BIOSIS DOCUMENT NUMBER: PREV200600212473

TITLE: Retinoic acid causes up-regulation of the gastrointestinal

glutathione peroxidase (GI-GPx) promoter and concomitantly down-regulation of hepatitis C virus (HCV) subgenomic RNA.

AUTHOR(S): Herget, T.; Morbitzer, M.; Klebl, B.; Galle, Peter; Becher,

Wulf; Wallasch, Christian

SOURCE: Gastroenterology, (APR 2005) Vol. 128, No. 4, Suppl. 2, pp.

A699.

Meeting Info.: Annual Meeting of the American-

Gastroenterological-Association/Digestive-Disease-Week. Chicago, IL, USA. May 14 -19, 2005. Amer Gastroenterol

Assoc.

CODEN: GASTAB. ISSN: 0016-5085.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Mar 2006

Last Updated on STN: 29 Mar 2006

The mRNA expression patterns of three Hepatitis C Virus (HCV)-subgenomic AR RNA replicon cell lines were compared with those of mock transfected or untransfected HuH7 cells utilizing cDNA array filters. The gastrointestinal-glutathione peroxidase (GI-GPx) mRNA was drastically down-regulated (as low as 5 to 10% of controls) in all replicon cell lines, while the expression level of the classical cellular-glutathione peroxidase (cGPx) remained unaffected. These data were confirmed by Northern blot and Western blot analyses. GI-GPx is a selenoprotein belonging to a family of four members, responsible for the detoxification of peroxides. Measuring total cellular glutathione peroxidase activity, revealed that the replicon cells showed reduced glutathione peroxidase activity (approx. 50% of control cells). Accordingly, replicon cells demonstrated increased susceptibility towards paraquat, a compound producing oxidative stress, reflected by a reduced viability of the replicon cultures compared to mock-transfected cell lines. When replicon cells were incubated with interferon for four days to induce the innate immune response, the HCV-replicon became down-regulated. Concomitantly, expression of CI-GPx resumed to nearly normal levels. Interferon itself did not effect the expression of GI-GPx in mock transfected and naive HuH7 cells. Furthermore, transient over-expression of the GI-GPx cDNA via adenoviral gene transfer induced a substantial and consistent down-regulation of the HCV RNA and the NS5a protein in replicon cells. In depth inspection of the 5' promoter region of the GI-GPx gene revealed the presence of two retinoic acid response elements (RARE). Treating replicon cultures with retinoic acid in the presence of selenite lead to increased expression of endogenous GI-GPx, followed by a dramatic down-regulation of the replicon. This decrease was even more pronounced, when cells were incubated with retinoic acid in the presence of selenite and interferon alpha. Taken together, these data show, that (a) expression of GI-GPx and replication of HCV exclude each other and (b) retinoic acid might be a valuable tool for the treatment Of HCV patients. Therefore, a clinical pilot trial at the University of Mainz with 9 population of interferon non-responders was initiated. Preliminary data of this clinical trial will be presented in parallel.

L18 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:569254 CAPLUS

DOCUMENT NUMBER: 131:331773

TITLE: Interferon/antioxidant combination therapy for chronic

hepatitis C- a controlled pilot trial

AUTHOR(S): Look, M. P.; Gerard, A.; Rao, G. S.; Sudhop, T.;

Fischer, H.-P.; Sauerbruch, T.; Spengler, U.

CORPORATE SOURCE: Department of General Internal Medicine, University of Bonn, Bonn, Germany

SOURCE: Antiviral Research (1999), 43(2), 113-122

CODEN: ARSRDR; ISSN: 0166-3542

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

hepatitis C.

The effects of two forms of antioxidative co-therapy were analyzed in 24 interferon-alpha (IFN)-naive patients with chronic hepatitis C who were randomized to either receive IFN monotherapy (3+4.5 million units IFN- α 2a per wk), (group A), or IFN and N-acetylcysteine (NAC) 1.800 mg/day plus sodium selenite (400 µg/day) supplementation (group B), or treatment as in group B plus vitamin E (544 IU/day) (group C), over 24 wk. Changes in histol., normalization of ALT, reduction of viral RNA, serum levels of glutathione, selenium, vitamin E, erythrocyte glutathione peroxidase, trolox equivalent antioxidative capacity (TEAC), thiobarbituric acid reactive substances (TBARS) and protein carbonyl groups were measured. Low baseline TEAC and elevated TBARS indicated increased oxidative stress before therapy, which was not affected by antioxidant supplementation. At the end of treatment complete responses were found in 3/8, 2/8 and 6/8 patients in groups A, B and C, resp., but liver histol. had not significantly improved. Vitamin E treated patients had a 2.4 greater chance (95% CI: 1.05-5. 5) of obtaining a complete response and had significantly greater reduction in viral load (P=0.028) than patients without vitamin E. Relapses, i.e. re-appearance of detectable hepatitis C virus (HCV) RNA and/or re-elevation of ALT-activity occurred in 7 out of the 11 responders within 6 mo after termination of therapy (group A: 2/3, group B: 1/2 and group C: 4/6). Thus, no overall beneficial effect of antioxidant/IFN therapy was detected. However, the apparent trend towards a more favorable outcome with vitamin E supplementation warrants to further study this substance as an adjuvant to IFN therapy in chronic

L14 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN

ACCESSION NUMBER: 1997:251696 BIOSIS DOCUMENT NUMBER: PREV199799550899

TITLE: Serum selenium, plasma glutathione (GSH) and

erythrocyte glutathione peroxidase

(GSH-Px)-levels in asymptomatic versus symptomatic human

immunodeficiency virus-1 (HIV-1)-infection.

AUTHOR(S): Look, M. P. [Reprint author]; Rockstroh, J. K.; Rao, G. S.;

Kreuzer, K.-A.; Barton, S.; Lemoch, H.; Sudhop, T.; Hoch,

J.; Stockinger, K.; Spengler, U.; Sauebruch, T.

CORPORATE SOURCE: Dep. General Internal Med., Univ. Bonn, Sigmund

Freud-Strasse 25, 53105 Bonn, Germany

SOURCE: European Journal of Clinical Nutrition, (1997) Vol. 51, No.

4, pp. 266-272.

CODEN: EJCNEQ. ISSN: 0954-3007.

DOCUMENT TYPE:

Article English

LANGUAGE: ENTRY DATE:

Entered STN: 13 Jun 1997

Last Updated on STN: 9 Jul 1997

Objectives: Antioxidant defense status was investigated in HIV-infected AB patients by measuring serum selenium, erythrocyte glutathione peroxidase (GSH-Px) activity, plasma thiol (-SH) and glutathione (GSH) concentrations along with the assessment of the clinical stage and surrogate markers of HIV-disease. Design, setting and subjects: Serum selenium levels were determined cross-sectionally in 104 sequentially selected HIV-infected patients (83 outpatients and 21 patients with ongoing AIDS defining events). The patients were classified into three stages of the disease, I, II and III according to the 1993 Centers For Disease Control (CDC) classification system for HIV-infection. GSH-Px activities, plasma SH and plasma GSH concentrations were determined in a subset of 24 patients at stage I and 12 patients at stage III with an active AIDS-defining disease. Mean serum selenium levels were lower in CDC stage I1 (68.7 +-20.9 mu-g/l; P lt 0.01; n = 34) and stage III (51.4 +- 14.7 mu-g/l; P lt 0.01; n = 37) HIV-infected patients than in healthy subjects (89.2 +- 20.9 mu-g/1; n = 72) and stage I patients (82.3 +- 20.5; mu-g/1; n = 33). Serum selenium levels were positively correlated with CD4- count (r = 0.42; P lt 0.001; n = 104) and inversely with levels of soluble tumor necrosis factor receptors type II (r= -0.58; P lt 0.01; n=35), neopterin (r = -0.5; P lt 0.001; n = 80) and beta-2-microglobulin (r = -0.4; P lt = -0.5; P lt = -0.5;0.001; n=94). Hepatitis C virus (HCV) and HIV-coinfected patients at CDC stages I and II showed markedly lower selenium concentrations compared to HIV-infected patients without concomitant HCV-infection. Serum selenium and GSH-Px activity in hospitalized AIDS patients was significantly lower as compared to asymptomatic patients and healthy subjects, whereas plasma SH and GSH concentrations were lower in both, asymptomatic -and AIDS-patients, than in the controls. Conclusion: The results show that stages I-III of HIV-disease are characterized by significant impairments of antioxidative defenses provided by selenium, GSH-Px, SH-groups and GSH.